Identifying and Managing Complications of Whole Brain Radiotherapy

Kathleen Madden, RN, MSN, FNP-BC, AOCNP®

S.D. is an 85-year-old man initially diagnosed in 1996 with a cutaneous malignant melanoma on his scalp. His disease has slowly progressed during the past several years, requiring multiple surgeries, localized scalp and neck irradiation, chemotherapy, and systemic biologic agents, with overall good systemic disease control. Six months ago, S.D. showed signs of clinical progression of subcutaneous disease of the left neck and axillae. Repeat computed tomography scans revealed overall progression of existing subcutaneous and pulmonary disease, and new brain lesions were discovered. Magnetic resonance imaging (MRI) with contrast revealed diffuse innumerable supratentorial brain metastases measuring 2–5 mm. The largest lesion was located in the right parietal lobe and measured 1.1 x 1 x 0.9 cm with surrounding vasogenic edema. Based on the large quantity of diffusely scattered lesions, stereotactic radiosurgery and surgical resection were not appropriate options. A course of whole brain radiation therapy (WBRT), delivering 37.5 gray over three weeks was deemed the best approach to palliate S.D.’s brain metastases.

Complications that developed during the first four months after irradiation had a significant impact on S.D.’s physical and neurocognitive function. Those complex yet often predictable problems are sequelae of WBRT and the medications necessary to manage disease- and treatment-related effects. The long-lasting, debilitating effects of therapy have proven to be very challenging for S.D., his wife, and the multidisciplinary team caring for him.

Patient Assessment

Prior to WBRT, S.D.’s performance status was 90 on a Karnofsky Performance Scale (KPS) and 28 of 30 on a Mini-Mental Status Examination (MMSE). His primary complaints were those of National Cancer Institute Common Toxicity Criteria for Adverse Events grade I fatigue, 3 of 10 left neck subcutaneous tumor pain, memory deficits, and generalized weakness. Upon diagnosis of the new brain metastases, a glucocorticoid steroid, dexamethasone 4 mg four times a day, and anti-epileptic levitiracetam 500 mg twice a day were started as a prophylaxis for disease and radiation-induced symptoms.

After completing WBRT, S.D. developed a number of anticipated complications and symptoms, including grade II–III fatigue, steroid myopathy, persistent generalized weakness, gait imbalance, anorexia, forgetfulness, mild headaches, and steroid-induced diabetes. However, he did not experience nausea, vomiting, or seizure activity, all of which commonly occur with the presence of brain metastases (Lovely, 2004).

Repeat MRIs two and three months after WBRT showed stable disease, but a mild increase in cerebral edema was noted and managed with an escalation in dexamethasone dosage. Attempts to taper and discontinue daily oral dexamethasone dosing had been problematic. A reduction of less than 4 mg daily exacerbated S.D.’s symptoms related to cerebral edema.

Etiology of the Problem

S.D. is one in an estimated 170,000 people annually living in the United States with cancer who have developed brain metastases from their primary tumors (Khosla, 2008; Majer & Samlowski, 2007). Melanoma ranks third in occurrence after lung cancer and breast cancer for the primary site of brain metastases (Majer & Samlowski). Patients with pulmonary metastases have a higher risk of metastatic cells traveling via arterial circulation to the brain. The location of metastatic deposits tends to correlate with the path of blood flow (Eichler & Loeffler, 2007; Kholsa). Metastatic lesions most commonly occur in the cerebrum (supratentorium) with an 80%–85% incidence, followed by the cerebellum (infratentorium) with a 10%–15% incidence, and the brain stem with a 3%–5% incidence (Khosla; Lovely, 2004) (see Figure 1). Multiple sites of metastases commonly are discovered within the brain versus a solitary metastatic lesion from melanoma. A solitary metastatic lesion may be treated with local irradiation or surgery; however, new tumors often develop, particularly if systemic disease is controlled poorly (Khosla).

The pathophysiologic changes associated with WBRT alter the endothelium of the vessels and cause demyelination...
of white matter, which leads to necrosis over months to years. The injuries can be quantified into three phases as listed in Table 1 (Baschnagel, Wolters, & Camphausen, 2008; Wefel, 2006).

### Management and Prophylactic Strategies and Outcomes

The inflammatory process of radiation stays in effect for approximately four to six weeks after irradiation therapy (Baschnagel et al., 2008). An anticipated decline in cognitive, neurologic, and physical function can be very apparent approximately two weeks after completion of WBRT. A follow-up MMSE was administered to S.D. at the end of the first month after WBRT; results yielded a 22 of 30, consistent with an expected decline. Readministration at months 3 and 5 showed improved scores leveling at 26 of 30. The score is consistent with expected outcomes—an initial decline in cognition, then a return toward baseline (Baschnagel et al.). S.D.’s KPS scores during months 2 and 3 had declined to 50 and 60, respectively. At month 6, his KPS is 70 and continues to show signs of ongoing improvement.

During the first six months following WBRT, S.D. has remained on an extended course of dexamethasone to manage his symptoms. Fatigue has been persistent throughout the trajectory of S.D.’s illness, which has required a multifaceted approach in managing and differentiating potential neurotoxic side effects because of medications versus organic symptoms of disease. Medication titration, including adjusting

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### Figure 1. Functional Geography of the Brain


- **Left temporal lobe:** Hearing, vision, smell, understanding, and memory of what is seen or heard; recognizing words; personality, behavior, and sexual behavior
- **Brain stem:** Breathing, heart rate, digestion, level of alertness, sleep, sweating, blood pressure, temperature, and balance
- **Cerebellum:** Balance, posture, and motor coordination including extremities, and some memory for reflex movements
- **Right temporal lobe:** Hearing, understanding, organizing, and concentrating on what is seen or heard; recognition of musical tones, music sounds, and nonspeech information (e.g., drawings). Long-term memory, personality, and behavior, including sexual behavior
- **Occipital lobe:** Accurately interpreting what is seen and visual images. Reading and writing, finding objects, identifying colors, recognizing words and drawn objects, and recognizing whether an object is moving
- **Parietal lobe:** Vision and sense of touch. Coordinating input from different senses for understanding, sensory control of the body, writing, mathematics, and language. Body positioning, handling of objects, and verbal and nonverbal memory
- **Frontal lobe:** Higher intellectual functions, such as consciousness and responses to outside stimuli; personality. Motor coordination for swallowing salivation, vocalization, chewing, facial expressions, as well as for hands, arms, torso, pelvis, legs, and feet
levatiracetam to 500 mg daily and tapering dexamethasone slowly to 1 mg daily, have proven helpful.

In addition to the reduction in steroid dosage, S.D. has been receiving an extended course of outpatient physical therapy incorporating instruction in techniques for energy expenditure and conservation. Physical therapy has been adjusted to his level of function and focuses on balance, coordination, stretching, range of motion, and gentle strengthening exercises. Maintaining muscle tone and preventing further loss of strength helps reduce the effects of steroid myopathy as well as better manage fatigue (Lovely, 2004). Considering S.D.’s prior neck irradiation, thyroid function tests were obtained to rule out another factor that might be contributing to his symptoms; results were normal.

An endocrinology referral was made to help manage S.D.’s steroid-induced diabetes. The oral medication glyburide was initiated and adjusted from 5–10 mg twice a day before meals according to blood glucose levels. Support from visiting nursing services was essential in teaching S.D. and his wife the importance of maintaining treatment compliance and safe management of glucose monitoring. Strategies to prevent further weight loss were addressed by the nutritionist and included dietary modifications and the addition of megace 400 mg oral suspension daily.

Between office appointments, oncology nursing staff kept in close contact by phone, providing many avenues of support for S.D. and his wife. They reassured, guided, and promoted S.D. and his wife’s confidence levels in their ability to learn new skills and techniques to manage S.D.’s care. Education in regard to the lengthy recovery process following WBRT has helped determine realistic goals and expectations of the standard course of recovery for S.D. and the need for flexibility when setbacks occur. Early symptom recognition and reporting is vital to optimal intervention and management. In addition, ongoing assessments conducted by oncology nurses have helped maintain patient safety at home and in the community. Palliating S.D.’s symptoms has limited dysfunction, contributing to overall better quality of life.

Table 1. Complications Related to Whole Brain Radiation Therapy (WBRT)

<table>
<thead>
<tr>
<th>PHASE</th>
<th>TIME</th>
<th>MECHANISM</th>
<th>SYMPTOMS</th>
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<tbody>
<tr>
<td>Acute</td>
<td>First two weeks of WBRT to one month after</td>
<td>Edema</td>
<td>Scalp and skin reaction, erythema, alopecia, fatigue, dizziness, nausea, ataxia, and exacerbation of focal neurologic deficits</td>
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<tr>
<td>Early</td>
<td>One to six months after WBRT</td>
<td>Edema and demyelination</td>
<td>Neurocognitive dysfunction; headache; impaired memory; executive dysfunction; alteration in attention, fine motor skills, and personality; seizures; and depression</td>
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<tr>
<td>Late</td>
<td>Six months to years after WBRT</td>
<td>Demyelination, vascular compromise, and necrosis</td>
<td>Seizures, leukoencephalopathy, memory changes, dementia (progressive), depression (progressive), and neuroendocrine dysfunction</td>
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Note. Based on information from Baschnagel et al., 2008; Wefel, 2006.

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